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Letter to the Editor

Urticaria multiforme: Two cases with histopathological findings

Dear Editor,

Urticaria Multiforme (UM) is a morphologic subtype of urticaria that usually affects infants and small children. It manifests with annular and polycyclic urticarial plaques with a violaceous center, and is often accompanied by acral edema and fever.[1]

We report two patients with this diagnosis, confirmed by the histopathological exam. The findings of the histopathology study are little described in previously published studies.

Case 1: A 15-month-old boy presented with a 4-day history of pruritic erythematous edematous plaques, some with dusky purple center, on the face, the trunk, arms and legs. The duration of individual urticarial lesions was less than 24 h. He received intramuscular penicillin G benzathine for pharyngitis one day prior to the onset of the cutaneous eruption. The initial hypotheses were acute urticaria, urticarial vasculitis and acute hemorrhagic edema of infancy. Complete blood count (CBC), erythrocyte sedimentation rate (ERS) and urinalysis were normal and C-reactive protein was 14,45 mg/ml (normal < 5,0 mg/ml). The histopathological exam showed epidermis preserved, dermis and superior hypodermis with perivascular and interstitial mixed infiltrate with eosinophils and neutrophils. These findings were suggestive of urticaria (Fig. 1). The patient was treated with oral corticosteroid and the lesions faded in a few days.

Case 2: A 40-day-old boy presented a 1-day history of annular, polycyclic, erythematous and edematous wheals, with a livid violet-colored central area on his face, trunk and limbs, associated with one fever peak of 38 °C (100.4 °F). His individual urticarial lesions had a fleeting nature, lasting less than 24 h before disappearing. He also presented edema of his hands and feet. The baby was exclusively breastfed and his mother had taken dipyrone (methimazole) one day prior to presentation. The initial hypotheses were acute urticaria, acute hemorrhagic edema of infancy and erythema multiforme. The skin biopsy revealed epidermis preserved, superficial and deep dermis with perivascular and interstitial mixed infiltrate with histiocytes, eosinophils and neutrophils, favoring urticaria (Fig. 2). CBC, ERS, urinalysis, blood and urine culture and C-reactive protein were normal. His disorder self-resolved in two days.

Discussion

UM was first described in 1997 as *acute annular urticaria*.[2] In 2007, Shah *et al.* introduced the term "urticaria multiforme", considering that this benign cutaneous hypersensitivity reaction is commonly confused with erythema multiform.[1] It is a clinical variant of urticaria and presents as an acute onset of arcuate, annular, polycyclic and erythematous plaques with central areas that are dusky, violaceous to brown colored.[1,3]

Usually, UM occurs between 4 months and 4 years of age,[1,4] although it was also reported in neonates and adults.[5,6] Some possible triggers have been suggested, including drugs (e.g., furazolidone, amoxicillin, nitrofurantoin), immunizations and some infections, such as pharyngitis, otitis media and upper respiratory infections.[1,2,4]

There are some differential diagnoses including erythema multiforme, serum-sickness-like reactions, urticarial vasculitis and acute hemorrhagic edema of infancy.[1,4,7,8] Erythema multiforme is the most common misdiagnosis, since the ecchymotic centers of the lesions of UM simulates the targetoid aspect of erythema multiforme. However, in UM patients we can not observe skin necrosis and blistering. Also, patients with UM can present dermatographism, pruritus, and the skin lesions are transient, with individual lesions lasting less then 24 h.[1,4,8] Patients with serum-sickness-like eruptions generally presents myalgia, arthralgia and lymphadenopathy, besides polycyclic urticarial wheals.[1] Urticarial vasculitis is a leukocytoclastic vasculitis, rarely reported in children. The individual urticarial lesions typically last longer than 24 h, are more associated with pain than pruritus and patients may present other signs and symptoms as fever, arthralgia, nephritis and uveitis.[4,7] Finally, acute hemorrhagic edema of infancy is a variant of cutaneous small vessels leukocytoclastic vasculitis, characterized for acral edema, fever and purpuric lesions in children younger than two years old. The lesions can assume an urticarial aspect, but are purpuric and last longer than in UM, leaving a residual hyperpigmentation.[4,7]

UM is considered by clinical grounds and is not recommended an extensive investigation of possible causal factors.[1,8] Histopathological exam shows the classical findings of a typical urticaria, revealing dermal edema with perivascular and interstitial lymphocytic infiltrate with eosinophils and sometimes neutrophils.[4,9] These findings easily distinguishes UM of its main differential diagnosis, erythema multiforme, whose histology shows epidermal necrosis and also edema of the papillary dermis with dilated capillaries. Treatment of UM consists by discontinuation of new and unnecessary drugs; use of H1 and H2 antihistamines may be helpful and oral corticosteroids can he introduced in more refractory cases.[1,3,4] The knowledge of this disease is important for physicians to avoid excessive investigation and treatments and to reassure parents about the benign nature of this condition. We are adding more two cases of UM, which reinforces that histopathological findings of this condition are similar to the ones of common urticarias.

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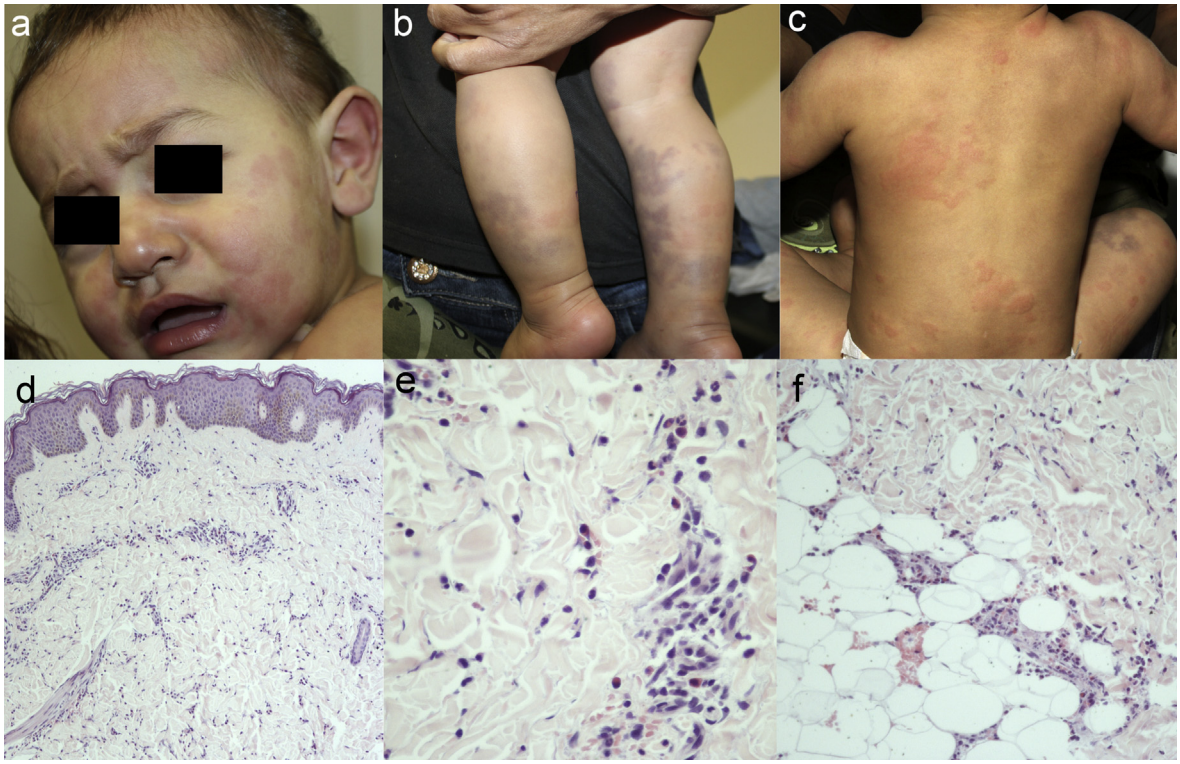

Fig. 1. Case 1: **a**, **b** and **c:** shows a 15-month-old boy with erythematous edematous plaques, some with dusky purple centers, on the face, legs and the trunk; **d:** 100× HE – shows epidermis preserved. Dermis and superior hypodermis with perivascular and interstitial mixed infiltrate with eosinophils and neutrophils; **e:** 400× HE – detail of the dermal infiltrate with eosinophils, neutrophils and extravasated erythrocytes; **f:** 200× HE – detail of the mixed infiltrate in the upper hypodermis.

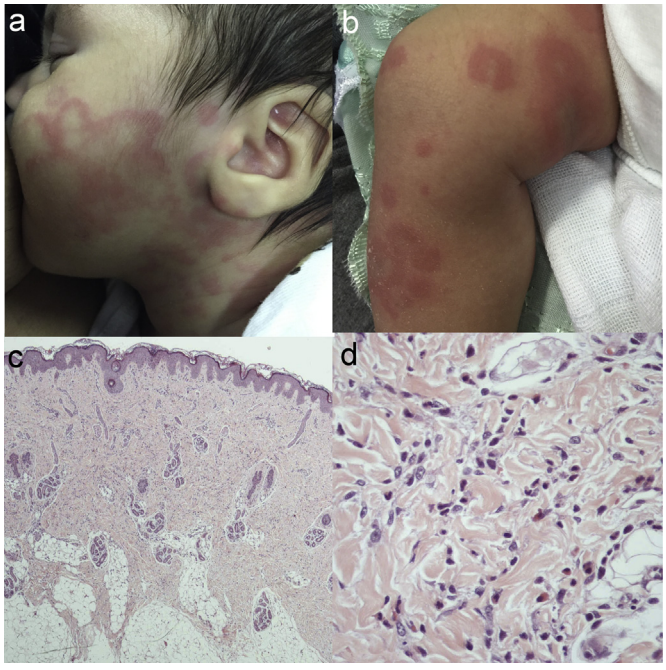

Fig. 2. Case 2: **a** and **b:** shows a 40-day-old boy with polycyclic urticarial plaques, some with dusky purple centers on the face and legs; **c:** 100× HE – shows epidermis preserved. Superficial and deep dermis with perivascular and interstitial mixed infiltrate with histiocytes, eosinophils and neutrophils; **d:** 400× HE – detail of the interstitial infiltrate with histiocytes, eosinophils and neutrophils.

Conflict of interest

The authors have no conflict of interest to declare.

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